

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

Applicant's or agent's file reference 47062.WO01	FOR FURTHER ACTION	See item 4 below
International application No. PCT/GB2005/000183	International filing date (<i>day/month/year</i>) 19 January 2005 (19.01.2005)	Priority date (<i>day/month/year</i>) 21 January 2004 (21.01.2004)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant CAMBRIDGE BIOTECHNOLOGY LIMITED		

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 *bis*.1(a).

2. This REPORT consists of a total of 10 sheets, including this cover sheet.

In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

- | | | |
|-------------------------------------|--------------|---|
| <input checked="" type="checkbox"/> | Box No. I | Basis of the report |
| <input type="checkbox"/> | Box No. II | Priority |
| <input checked="" type="checkbox"/> | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| <input checked="" type="checkbox"/> | Box No. IV | Lack of unity of invention |
| <input checked="" type="checkbox"/> | Box No. V | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input type="checkbox"/> | Box No. VI | Certain documents cited |
| <input type="checkbox"/> | Box No. VII | Certain defects in the international application |
| <input type="checkbox"/> | Box No. VIII | Certain observations on the international application |

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis .2).

<p style="text-align: center;">The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland</p> <p>Facsimile No. +41 22 338 82 70</p>	<p>Date of issuance of this report 24 July 2006 (24.07.2006)</p> <p>Authorized officer <div style="text-align: center;">Nora Lindner</div></p> <p>e-mail: pt02@wipo.int</p>
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PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

REC'D 06 MAY 2005

WIPO PCT

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To:

see form PCT/ISA/220

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/GB2005/000183

International filing date (day/month/year)
19.01.2005

Priority date (day/month/year)
21.01.2004

International Patent Classification (IPC) or both national classification and IPC
C07H19/16

Applicant
CAMBRIDGE BIOTECHNOLOGY LIMITED

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/GB2005/000183

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
☐ a sequence listing
☐ table(s) related to the sequence listing
 - b. format of material:
☐ in written format
☐ in computer readable form
 - c. time of filing/furnishing:
☐ contained in the international application as filed.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/GB2005/000183

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,
- ☒ claims Nos. 17

because:

- ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):
- ☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 17 are so unclear that no meaningful opinion could be formed (*specify*):

see separate sheet

- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the whole application or for said claims Nos.
- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

- ☐ has not been furnished
- ☐ does not comply with the standard

the computer readable form

- ☐ has not been furnished
- ☐ does not comply with the standard

- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.
- ☐ See separate sheet for further details

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/GB2005/000183

Box No. IV Lack of unity of invention

1. ☐ In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has:
- ☐ paid additional fees.
 - ☐ paid additional fees under protest.
 - ☐ not paid additional fees.
2. ☒ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is
- ☐ complied with
 - ☒ not complied with for the following reasons:
see separate sheet
4. Consequently, this report has been established in respect of the following parts of the international application:
- ☒ all parts.
 - ☐ the parts relating to claims Nos.

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, Inventive step or Industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-8,10-14,16,18-19
	No: Claims	9,15,20
Inventive step (IS)	Yes: Claims	1-8,10-12,16,18-19
	No: Claims	9,13,14,15,20
Industrial applicability (IA)	Yes: Claims	1-20
	No: Claims	---

2. Citations and explanations

see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The wording of claim 17 ("..substantially as described with reference to..") is vague and unclear and leaves the reader in doubt as to the meaning of the technical features to which it refers, thereby rendering the definition of the subject-matter of said claim unclear, Article 6 PCT.

Therefore claim 17 will not be examined.

Re Item IV

Lack of unity of invention

The following document are cited :

- D1: BROWN, GEORGE BOSWORTH ET AL: "2- Chloroadenine and 2-chloroadenosine" JOURNAL OF ORGANIC CHEMISTRY (1958), 23, 125-6
CODEN: JOCEAH; ISSN: 0022-3263, 1958, XP002325338
- D2: BERGMANN W ET AL: "CONTRIBUTIONS TO THE STUDY OF MARINE PRODUCTS. XLIII. THE NUCLEOSIDES OF SPONGES. V. THE SYNTHESIS OF SPONGOSINE" JOURNAL OF ORGANIC CHEMISTRY, AMERICAN CHEMICAL SOCIETY. EASTON, US, vol. 22, December 1957 (1957-12), pages 1575-1577, XP001205635 ISSN: 0022-3263

This Authority considers that there are 3 inventions covered by the claims indicated as follows:

- I: Claims 1-8,10,12(part),13(part),14(part),16-20 directed to a process for the preparation of spongosine.
- II: Claims 9,11,12(part),13(part),14(part) directed to a process for the preparation of 2-methoxyadenine.
- III: Claims 15 directed to a process for the preparation of the intermediate compound

2-chloro-adenine.

The reasons for which the inventions are not so linked as to form a single general inventive concept, as required by Rule 13.1 PCT, are as follows:

The subject-matter of the present application concerns the synthesis of spongosine. The intermediate compounds 2,6-dichloropurine, 2-chloroadenine and 2-methoxyadenine (and a process for the preparation thereof) are already known (see D1-D2).

The common concept linking the 3 above-mentioned inventions being known, the Examiner considers that these 3 inventions are not so linked as to form a single general inventive concept.

The application, hence does not meet the requirements of unity of invention as defined in Rules 13.1 and 13.2 PCT.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Invention I :

Novelty :

The subject-matter of invention I concerns a process for the preparation of spongosine comprising reacting 1-O-acetyl-2,3,5-tri-O-benzoyl- β -D-ribofuranose with 2-methoxyadenine followed by deprotection of the resulting compound to obtain spongosine.

- a) Since purity is not a valid criterion to acknowledged novelty, the subject-matter of claim 20 in not considered new contrary to Art 33(2) PCT.
- b) Since none of the available prior art discloses this process, the subject-matter of 1-8,10,12(part),13(part),14(part),16-19 is considered new according to Art. 33(2) PCT.

Inventive step :

Since none of the available prior art suggest the direct coupling of the protected ribose with 2-methoxyadenosine, the subject-matter of claims 1-8,10,12(part),13(part),14(part),16-19 is considered inventive according to Art. 33(3) PCT.

Industrial application :

The subject-matter of invention I complies with the requirements of Art. 33(4) PCT.

Invention II :

The subject-matter of invention II concerns a process for the preparation of 2-methoxyadenine comprising heating 2-chloroadenine with sodium methoxide/methanol to less than 150 °C.

Novelty :

Claim 9 :

D2 discloses the same reaction performed at 150 °C (see page 1576 left-hand column bottom). As there is always a margin of error when performing a reaction at a certain temperature (usually from 0.5 to 1 °C), the Examiner considers that the subject matter of claim 9 overlaps this range. Hence the subject-matter of claim 9 is not considered new contrary to Art. 33(2) PCT.

Claims 11,12(part),13(part),14(part) :

Since none of the available prior art discloses the subject-matter of claims 11,12(part),13(part),14(part), said claims are considered new according to Art. 33(2) PCT.

Inventive step :

Claim 13-14 :

Since 2,6-dichloropurine is a known potential precursor of 2-chloroadenine, claim 13-14 are considered as an obvious combination of D2 and D1.

Claims 11-12 :

Since none of the available prior art suggest the subject-matter of claims 11-12, said claims are considered inventive according to Art. 33(3) PCT.

Industrial application :

The subject-matter of invention II complies with the requirements of Art. 33(4) PCT.

Invention III :

Novelty :

The subject-matter of invention III concerns a process for the preparation of 2-chloroadenine comprising treating 2,6-dichloropurine with methanolic ammonia to produce 2-chloroadenine, diluting the 2-chloroadenine produced with water and isolating the compound.

D1 discloses a process for the preparation of 2-chloroadenine comprising treating 2,6-dichloropurine with methanolic ammonia to produce 2-chloroadenine, evaporating the supernatant, then diluting the 2-chloroadenine produced with 1N NaOH (therefore with water) and isolating the compound.

Thus D1 anticipates the subject-matter of invention III.

Industrial application :

The subject-matter of invention III complies with the requirements of Art. 33(4) PCT.

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/GB2005/000183